PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference P818PC00	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/DK2004/000634	International filing date *(day/month/year)* 17 September 2004 (17.09.2004)	Priority date *(day/month/year)* 19 September 2003 (19.09.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant LEUKOTECH A/S		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 21 March 2006 (21.03.2006)
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

31/3

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK2004/000634	17.09.2004	19.09.2003

International Patent Classification (IPC) or both national classification and IPC
C07K16/18, A61K39/395

Applicant
LEUKOTECH A/S

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DK2004/000634

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/DK2004/000634

Box No. II Priority

1. ☐ The following document has not been furnished:

   ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 29-39

because:

☒ the said international application, or the said claims Nos. 29-39, with regard to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	21-24,26-41
	No:	Claims	1-22,25
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-41
Industrial applicability (IA)	Yes:	Claims	1-28, 40,41
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 29-39 encompass methods of treatment of the human or animal body, and thus relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Document D1 (WO-A-00/66151) discloses (see e.g. claims 26-29) pharmaceutical compositions comprising an antibody against hHBP (which will bind to an epitope either in the amino acid sequence 1-19, 20-44 or 45-226).

   Similarly, D2 (WO-A-93/19087) discloses (see e.g. page 3, lines 2-6, page 17, 1-30 and pages 58-59) pharmaceutical compositions comprising an antibody against hHBP (= CAP37).

   In addition, D3 (US-B-6,468,533) discloses (see e.g. claim 1 and column 2 lines 31-32) pharmaceutical compositions comprising an antibody against HMG1, i.e. a homologue of hHBP.

1.1 The subject-matter of independent claim 1, which is a claim of the "first medical use" type, is hence not novel over the disclosures of D1-D3 in the sense of Article 33(2)

PCT.

1.2 A similar argumentation also applies for the subject-matter of dependent claims 2-22, wherein the antibodies are further defined by intrinsic features, which subject-matter is not considered to be novel in the sense of Article 33(2) PCT.

2. None of the prior art documents at hand discloses the specific monoclonal antibodies defined in independent claims 21 and 22.
However, for the person skilled in the art, the production of alternative antibodies to a known antigen according to standard protocols does not require an inventive activity. Therefore, the antibodies proposed in independent claims 21 and 22 cannot be considered as meeting the requirements of Article 33(3) PCT with regard to inventive step.
In such a case, inventiveness could only be recognised if said alternative antibodies would display unexpected properties or effects (see also the PCT Guidelines, 13.14).

2.1 A similar argumentation also applies for the subject-matter of independent claims 23 and 24. The subject-matter of these claims is hence not inventive in the sense of Article 33(3) PCT.

3. As presented herein-above, D1-D3 disclose antibodies falling within the scope of independent claim 25. The subject-matter of said independent claim 25 is thus not novel in the sense of Article 33(2) PCT.

3.1 Similarly, the subject-matter of independent claims 26-28 is not considered to be inventive in the sense of Article 33(3) PCT.

4. The teachings of D1-D3 relate indirectly to inflammation, since it was well known that hHBP is related to the inflammatory process, see e.g. D4 (US-B-5,650,392), D5 (FEBS Letters, 1996, **390**:109-112), D6 (International Journal of Surgical Investigation, 2001, **2**(6):457-466) or D7 (Journal of Surgical Research, 2000, **89**:53-

59). Moreover, D4 teaches (see e.g. column 4, line 41 - column 6, line 50, and claims) that a peptide comprising amino acids 20-44 of hHBP has particular properties as compared to the rest of the protein.
The use of the antibodies of D1-D3 in order to modulate inflammatory responses as claimed in claims 29-41 is therefore not considered to be inventive in the sense of Article 33(3) PCT.

Additional comments

5. Claims 21 and 22 are found twice (dependent claims 21 and 22, as well as independent claims 21 and 22) in the present set of claims (Article 6 PCT).

5.1 Features placed between brackets are optional. The antibodies of independent claims 21 and 22 are hence only defined by trivial names, which are deemed to be unclear for the skilled person. Claims 21 and 22 EPC hence do not fulfill the requirements of Article 6 PCT.

5.2 A similar objection (Article 6 PCT) also applies for the subject-matter of independent claim 31 and 32 and of independent claims 40 and 41.

5.3 Moreover, the fragments claimed in independent claims 31 and 32 are any fragments and appear to encompass known fragments, e.g. the Fc part of the antibodies (Article 6 PCT).

6. For the assessment of the present claims 29-39 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 2004/016653	26.02.2004	14.08.2003	15.08.2002

Should the present application enter the national or regional phase, the above cited document could be relevant for the question of novelty.